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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/604,022	COLLINS ET AL.	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 and 4-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the reply received June 23, 2007.

Claims 1-2 and 4-12 are pending in the application.

Any rejection from the previous office action, which is not restated here, is withdrawn.

Applicant has now amended the base claim to recite an extra step (a) transferring solid phase resin between a resin source external to a single microwave transparent vessel and the microwave transparent vessel. Claims 1-2 and 4-12 are presented for examination on the merits.

Rejections withdrawn

Claim Rejections - 35 USC § 112

The previous rejection of claims 1-2 and 4-12 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn for the following reason: Applicant's arguments substantiating that 1) the skilled person understands quite well the meaning of terms such as "microwave", "microwave transparent" and "vessel" and 2) in addition to the understanding that the skilled person brings, the pending specification uses these well-understood terms to describe the invention in a manner that is above and beyond the minimum requirements of the112 1st written description requirement, have been deemed persuasive.

Rejections maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1 and 4 are rejected under 35 U.S.C. 102(a) or under 102(e) as being anticipated by Martin et al. (US 2003/0082633) as evidenced by Hilpert et al. (Protein Engineering, 2001).

Martin et al. teach a process for the solid phase synthesis of peptides (EQKLISEEDL and EQKHISEEDL) in a single vessel (e.g., Example 12-13) and shortening reaction times by a factor of 2-20 fold by the use of the microwave energy

during the reactions (e.g., Example 12, [0294]-[0300]). Hilpert et al. teach that the peptides of Martin et al. were synthesized via a cellulose-bound C-terminus with two β-alanine as a spacer (e.g., column 2, lines 16-18) and following a protection/deprotection scheme (e.g., column 2, lines 12-17) and therefore would inherently encompass the instantly claimed standard solid phase peptide synthetic steps. Please note that the limitation "in a single vessel without removing the peptide from the single vessel between cycles" is met by the fact that the peptides are chemically bound to the cellulose during synthesis (e.g., Martin et al. Example 12, [00295], lines 1-8), which is glued on top of a sandwich comprising two standard glass microscope slides (a microwave transparent material) and the edges are sealed to enclose barium titanate (a microwave susceptor). The vessel therefore reads upon a microwave transparent vessel and upon a microwave susceptor vessel. Therefore, the reference is deemed to anticipate the instant claims above.

Applicant's arguments

The rejections are inappropriate for at least 2 reasons: (1) Martin '633 fails to disclose the claimed invention within its four corners; and (2) the relevant portions of Martin '633 lack enablement and thus cannot support any art-based rejection against the pending claims.

Claim 1 has been amended to recite the step of transferring solid phase resin between a resin source external to a single microwave transparent vessel and the

microwave transparent vessel. This now appears as the initial step "(a)" in Claim 1, with the remaining steps being re-phrased appropriately in sequence.

This step, which is taken from Paragraphs 0038 and 0046 of the specification as filed, further differentiates the claimed invention from Martin. In the office actions dated December 15, 2006 and March 23, 2007 (e.g., page 8), the Examiner has taken the position that when a peptide is bound to Martin's glass and susceptor sandwich, the glass and susceptor sandwich is deemed to be a "vessel".

Martin describes (e.g., Paragraph 0295) a sandwich formed of an aqueous paste of barium titanate between two standard glass microscope slides. A cellulose membrane is glued to one of the slides. The peptide precursors are added as spots onto the cellulose membrane. According to the Examiner, Claim 1's recitation of a microwave transparent vessel reads upon Martin's combination of paper, glass, ceramic and glue. The Examiner also takes the position that Martin's sandwich is concurrently microwave transparent and microwave absorbing. Microwave transparency and absorbency are opposite functions and only one of them --transparency—is recited in Claim 1.

Applicants have previously argued that any analogy between a vessel and Martin's sandwich is tenuous at best. Nevertheless, in order to clarify Claim 1, the step of transferring solid phase resin from an external source into the vessel has been added. As noted in previous responses and elsewhere herein, if Martin's sandwich is the "vessel", then it cannot serve as the "resin" and vice versa. Furthermore, Martin's

glass/ceramic/glass/cellulose sandwich cannot be added to itself in the manner than actual resin can be added to an actual vessel as now recited in Claim 1.

Also, in order for a reference to anticipate, the reference must enable the subject matter for which is being asserted. In turn, enablement requires that the reference teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation. The disclosure in the anticipating reference must be adequate to enable possession of the desired subject matter. Naming or describing subject matter is insufficient if the subject matter cannot be produced without undue experimentation.

In making the anticipation argument, the office action cites (on page 7) a portion of Martin's Examples 12 and 13 and Paragraphs 0294-0300. This argument requires both cross reference to, and incorporation of the Hilpert publication and the Sigma-Genosys notes. In the response filed February 15, 2007, Applicants have pointed out the ambiguities raised by (1) Martin's lack of explicit explanation and (2) Martin's brief referral to Hilpert and Sigma-Genosys. The Examiner dismisses these problems with the unsupported conclusion that "one of ordinary skill in the art would understand how to use the claimed invention based on the skill in the art and upon the disclosure of Martin including citations therein." Therefore, because Martin fails to include, either explicitly or inherently, the elements recited in the claim 1, Martin cannot serve as 102 reference against Claim 1.

Response to Arguments

Applicant's arguments have been carefully considered but not deemed persuasive because 1) the term "microwave transparent vessel" is not defined in the disclosure and as written it does not exclude the vessel from having portions that may not be transparent, in other words, applicant is arguing a limitation that is not recited in the claim; 2) with regards to the vessel, the vessel is the sandwich comprising two standard glass microscope slides (a microwave transparent material) and the edges are sealed to enclose barium titanate to form a "sandwich dielectric chip", i.e., the vessel. The cellulose membrane which contains four acceptor spots for peptide synthesis reads upon the solid phase resin (e.g., Martin et al. Example 12, [00294]-[00298]). The cut-to-fit cellulosic "SPOTS" membrane is glued around the edges on the surface of the "sandwich dielectric chip" (i.e., the vessel). Therefore, the process of cutting and attaching the cellulosic SPOTS membrane (solid phase resin) by gluing to the "sandwich dielectric chip" (vessel) reads upon the newly added limitation "transferring solid phase resin between a resin source external to a single microwave transparent vessel and the microwave transparent vessel". Please note that Sigma-Genosys was not cited in the rejection and that Sigma-Genosys is a company that one skilled in the art would have been able to refer to at the time the invention was made by Martin. Martin teaches that "solid phase microwave chemistry is well known in the field" ([00295]). Upon further searching Examiner has been able to find a SPOTS FAQ dated 05/14/2002 about SPOTS at http://web.archive.org/web/20020514031700/www.sigma-genosys.com/peptide_faq.asp, which is herein cited and provided to Applicants.

Although this is not the "technical notes", the citation does disclose some details of the SPOTS peptide synthesis technique, including some of the steps therein (e.g., Fmoc synthesis, protection, deprotection, coupling) at the time the invention was made. Please also note that several peptides were successfully synthesized (Martin [00296]) via this procedure, and it is therefore, enabled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) in view of Williams (US 6,858,434) and in view of Martin et al. (US 2003/0082633).

Yu et al. teach a process for the solid phase synthesis of peptides, which comprises:

(a) deprotecting a first amino acid linked to a solid phase resin by removing protective first chemical groups;

(b) activating chemical groups on a second amino acid to prepare the second amino acid for coupling with the first amino acid;

c) coupling the activated second amino acid to the deprotected first amino acid to form a peptide from the first and second amino acids; and

(d) accelerating at least the coupling step by applying microwave energy during the coupling step. (see, e.g., page 4782-4784, Figures 1-2 and Scheme 1).

Yu et al. do not teach accelerating the deprotecting step by applying microwave energy during the deprotecting step or carrying out the reaction in a single vessel without removing the peptide from the single vessel between cycles.

Williams teaches deprotecting n-Boc protected amino acids by applying microwave energy during the deprotecting step (e.g., Example 5).

Martin et al. is relied upon as above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase microwave method of Yu et al. by carrying out the reaction on a cellulosic membrane to which the peptide to be synthesized is attached, as taught by Martin et al. (See, e.g., [294]-[301]) and accelerating the synthesis steps including deprotecting steps (as taught by Williams) with microwaves (See, e.g., Martin et al., column 23, [294]-[301]). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time as taught by Yu et al. (page 4781, column 1, lines 13-15) and by Williams (Example 5). There would have been a reasonable expectation of success, given the successful synthesis in a single microwave transparent vessel of the peptides: EQKLISEEDL and EQKHISEEDL as

taught by Martin et al. (e.g., Examples 12-13). Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 5, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) (Tetrahedron Letters, 2001) in view of Stadler et al. (Eur J Org Chem, 2001) in view of Santagada et al. (Tetrahedron Letters, 2001, citation 4 in the IDS of November 8, 2004) and in view of Martin et al. (US 2003/0082633).

Yu et al., Williams and Martin et al. are relied upon as above.

Yu et al. Williams and Martin et al. do not expressly teach accelerating the deprotecting step by applying microwave energy during the deprotecting step, maintaining the peptide in a single vessel during the process proactively cooling the vessel and its contents during application of microwave energy, cleaving the peptide from the resin applying microwave energy, deprotecting side chains of the peptide, spiking the microwave energy, using phosphorium activators, uranium activators, HATU, HBTU, PyBOP, PyAOP or HOBT, monitoring the temperature of the vessel and moderating the applied power accordingly.

Stadler et al. teach cleaving various molecules including carboxylic acids from resins by applying microwave energy, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power

accordingly (see, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2).

Santagada et al. teach using PyBOP/HOBt and HBTU/HOBt activators in a microwave method for peptide synthesis (see, e.g., pages 5171-5173).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the microwave method of Yu et al. by also accelerating the deprotecting steps in general during peptide synthesis with microwaves based on the teachings of Williams (See, e.g., Examples 5 and 7), by accelerating the cleavage from the solid-support resin as taught by Stadler et al. (See, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2), and by using activators such as PyBOP/HOBt and HBTU/HOBt during microwave activation, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly, as taught by Santagada et al. (See, e.g., pages 5171-5173). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time (e.g., Yu et al. page 4781, column 1, lines 13-15) and provide higher yields (e.g., Santagada et al. abstract). There would have been a reasonable expectation of success, given the successful synthesis in a single microwave transparent vessel of the peptides: EQKLISEEDL and EQKHISEEDL as taught by Martin et al. (e.g., Examples 12-13). The adjustment of particular conventional working conditions (e.g., deprotecting protective groups other than n-Boc in peptides, and alpha-amino groups or side chains

of the peptide) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim 1 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) in view of Williams (US 6,858,434) and in view of Cargill et al. (US 6,171,555).

Yu et al. teach a process for the solid phase synthesis of peptides, which comprises:

(a) deprotecting a first amino acid linked to a solid phase resin by removing protective first chemical groups;

(b) activating chemical groups on a second amino acid to prepare the second amino acid for coupling with the first amino acid;

c) coupling the activated second amino acid to the deprotected first amino acid to form a peptide from the first and second amino acids; and

(d) accelerating at least the coupling step by applying microwave energy during the coupling step. (see, e.g., page 4782-4784, Figures 1-2 and Scheme 1).

Yu et al. do not teach accelerating the deprotecting step by applying microwave energy during the deprotecting step or carrying out the reaction in a single vessel without removing the peptide from the single vessel between cycles.

Williams teaches deprotecting n-Boc protected amino acids by applying microwave energy during the deprotecting step (e.g., Example 5).

Cargill et al. teach a process for the solid phase synthesis of peptides in a single vessel (column 1, lines 38-67; column 2 and column 3, lines 1-30) using microwaves (e.g., column 4, lines 37-39) in a single microwave transparent vessel (e.g., column 4, lines 15-24, Figures 1; column 4, lines 25-39, Figure 2 and column 4, lines 43-67).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase microwave method of Yu et al. by carrying out the reaction in a single microwave transparent vessel as taught by Cargill et al. (e.g., column 4, lines 15-24, Figures 1; column 4, lines 25-39, Figure 2 and column 4, lines 43-67) and accelerating the synthesis steps including deprotecting steps (as taught by Williams) with microwaves (See, e.g., Cargill et al.). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time as taught by Yu et al. (page 4781, column 1, lines 13-15), by Williams (Example 5) and by Cargill et al. (e.g., column 4, lines 37-39). There would have been a reasonable expectation of success, given that libraries of peptides comprising single-vessel solid phase strategies were known to successfully synthesize simultaneously (one per vessel) a multitude of different peptides in a single run (e.g., Cargill et al., column 1, lines 38-67 and column 2, lines 1-20). Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 5, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004), in view of Williams (US 6,858,434), in view of Cargill et al. (US 6,171,555), in view of Stadler et al. (Eur J Org Chem, 2001) in view of Santagada et al. (Tetrahedron Letters, 2001, citation 4 in the IDS of November 8, 2004.

Cargill et al., Yu et al. and Williams are relied upon as above.

Cargill et al., Yu et al. and Williams do not expressly teach accelerating the deprotecting step by applying microwave energy during the deprotecting step, maintaining the peptide in a single vessel during the process proactively cooling the vessel and its contents during application of microwave energy, cleaving the peptide from the resin applying microwave energy, deprotecting side chains of the peptide, spiking the microwave energy, using phosphorium activators, uranium activators, HATU, HBTU, PyBOP, PyAOP or HOBT, monitoring the temperature of the vessel and moderating the applied power accordingly.

Stadler et al. teach cleaving various molecules including carboxylic acids from resins by applying microwave energy, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly (see, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2).

Santagada et al. teach using PyBOP/HOBt and HBTU/HOBt activators in a microwave method for peptide synthesis (see, e.g., pages 5171-5173).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the microwave method of Yu et al. by also accelerating the deprotecting steps in general during peptide synthesis with microwaves based on the teachings of Williams (See, e.g., Examples 5 and 7), by accelerating the cleavage from the solid-support resin as taught by Stadler et al. (See, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2), and by using activators such as PyBOP/HOBt and HBTU/HOBt during microwave activation, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly, as taught by Santagada et al. (See, e.g., pages 5171-5173). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time (e.g., Yu et al. page 4781, column 1, lines 13-15 and Cargill et al. column 4, lines 38-40) and provide higher yields (e.g., Santagada et al. abstract). There would have been a reasonable expectation of success, given that libraries of peptides comprising single-vessel solid phase strategies were known to successfully synthesize simultaneously (one per vessel) a multitude of different peptides in a single run as taught by Cargill et al. (e.g., column 1, lines 38-67 and column 2, lines 1-20). The adjustment of particular conventional working conditions (e.g., deprotecting protective groups other than n-Boc in peptides, and alpha-amino groups or side chains of the peptide) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus the invention as a whole was

clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments

First, Applicants repeat and reincorporate in their entirety the arguments filed on February 15, 2007. In brief, they include the following:

1) The Sigma-Genosys technical notes fail to appear in the IDSs filed by Martin or in the PTO-892s provided by the Office (in the Martin '633 prosecution history). The Examiner has neither provided them to the Applicants nor included them as a cited reference in any office action. The failure to provide the Applicants with a copy of the Sigma Genosys technical notes is inconsistent with the requirements of MPEP 707.05 (a) and (d). Accordingly, neither the Applicants nor the skilled person in the art can confirm the identity or contents of the Sigma-Genosys technical notes. Therefore, they cannot provide the foundation for using Martin '633 in any type of art-based rejection.

2. The Hilpert reference fails to explicitly disclose the peptide preparation process.

3. Because of the multiple ambiguities in the manner in which Martin incorporates Hilper and Sigma-Genosys and the manner in which Hilpert incorporates the two Kramer references, Martin '633 offers the skilled person at least six (6) permutations for carrying out Examples 12 and 13.

4. The large number of permutations that arise from the Examiner's use of Martin '633, Hilpert, Sigma-Genosys, Kramer and Kramer-Schneider, the Martin '633

publication cannot enable the claimed invention and thus must fail as prior art for such purpose.

5. Martin absorbs microwaves while claim 1 recites a vessel that transmits microwaves.

6. The Kramer-Schneider reference is inconsistent with the HMP resin techniques of Yu and fails to disclose or suggest the use of a microwave transparent vessel or microwaves to accelerate any of the relevant steps.

7. Three of the cited techniques (Yu, Williams, Martin) differ fundamentally from one another and cannot be logically combined other than as an attempt to reconstruct Claim 1 in hindsight.

8. The Examiner's position requires Martin's cellulose membrane to serve as both the linked solid phase resin (Claim 1, paragraph (a)) –and as the microwave transparent single vessel (Claim 1, paragraph (e))—which it is likewise not. The Examiner is taking a single element from the prior art and applying it to multiple different elements in Claim 1 on an ad hoc, as needed basis. The Examiner is stating, without support, that a cellulose membrane can be a linked solid resin peptide if necessary, or a single vessel if necessary, or both at the same time if necessary.

9. Claim 1 recites that the solid phase resin is linked to a first amino acid. If (as the Examiner asserts) the linked resin is the same as the single vessel, then the linked peptide would need to be in the vessel and be the vessel at the same time. This is logically inconsistent.

In addition to repeating previous 103 rejections, the Examiner has applied several new 103 rejections based on Yu and that include Willimas, Santagada, Stadler and Cargill as secondary references.

Applicants specifically repeat the points made in prior responses about combinations of Yu with Williams. Namely, Yu carries out peptide synthesis on a solid phase polystyrene resin, but fails to disclose or suggest deprotection using microwaves.

Williams avoids using a solid phase resin (thereby differing from both Claim 1 and Yu) and instead uses thin layer chromatography plates coated with silica gel. Accordingly, no reason exists to carry out the Williams technique on Yu's polysterene resin or the Yu technique on William's silica gel. The combination thus stands as a mere hidndsight reconstruction based upon Claim 1.

Accordingly, the "new rejections" based on combinations of Yu and Willimas must fail as lacking any logical support other than the pending claims.

The Santagada reference has been applied for the use of specific activators ina single microwave enhanced coupling reaction. Accordingly, regardless of the combination in which it is used, Santagada offers no cure for the weakenesses in the base references or the combinations.

The Examiner has cited Cargill US 6,171,55 for the first time in this office action. In its own words, Cargill illustrates, "a docking station (that) includes remotely actuated locking mechanisms for secure registration of reaction blocks, and provides for introduction of gases, liquids and vacuum to the reaction blocks" (e.g., Abstract). According to the Examiner, Cargill teaches solid phase synthesis of peptides in a single

microwave-transparent vessel using microwaves. The cited portions, however, offer little or no support to the Examiner's arguments. First, at cited column 1, lines 38-67, Cargill does nothing more than point out the same prior art that the pending specification pointed out when filed: i.e., peptides have historically been synthesized on solid phase resins. The Examiner also cites "column 2" but there appears to be nothing there that specifically applies to the claimed invention or to the Examiner's arguments other than a continuation of the background discussion of column 1.

The Examiner cites column 3, lines 1-30, but again this is a general discussion that neither applies to the pending claims nor supports any arguments based on the other references. The Examiner cites column 4, lines 37-39, 25-39 and 43-67, but these offer nothing other than the broad statement that in the Cargill docking station, "product reaction could be enhanced by the application of microwaves". Cargill fails to offer this in connection to any specific chemical reaction, but only as a general statement. Applicant accordingly submits that Cargill cannot cure the weaknesses of the combinations set forth in this office action. The remainder the claims are dependent from Claim 1, and thus all of the same arguments apply. Because these combinations fail to render Claim 1 obvious, they likewise fail to render any of the dependent claims obvious.

Response to Arguments

With regards to the arguments in 1) above, MPEP 707.05 (a), which was cited by Applicant discloses that:

"Copies of foreign patent documents and nonpatent literature (NPL) which are cited by the examiner at the time of allowance will be furnished to applicant with the Office action, and copies of the same will also be retained in the file. For

> Image File Wrapper (IFW) processing, see IFW Manual section 3.7. This will apply to all allowance actions, including first action allowances and Ex Parte Quayle actions. In the rare instance where no art is cited in a continuing application, all the references cited during the prosecution of the parent application will be listed at allowance for printing in the patent."

MPEP 707.05 (d), which was also cited by Applicant in connection with the rejections above reads:

> "Where an applicant in an amendatory paper refers to a reference that is subsequently relied upon by the examiner, such reference shall be cited by the examiner in the usual manner using a form PTO-892, "Notice of References Cited," unless applicant has listed the reference on a form ** PTO/SB/08 that has been initialed by the examiner."

In the instant case, the Sigma-Genosys was not cited by examiner since it was not used in any of the rejections and therefore the MPEP citations of Applicant do not apply. Upon further searching Examiner has been able to find a SPOTS FAQ dated 05/14/2002 about SPOTS at http://web.archive.org/web/20020514031700/www.sigma-genosys.com/peptide_faq.asp, which is herein cited and provided to Applicants. Although this is not the "technical notes", the citation does disclose some details of the SPOTS peptide synthesis technique, including some of the steps therein (e.g., Fmoc synthesis, protection, deprotection, coupling) at the time the invention was made. With regards to 2) the Hilpert reference is not mentioned as disclosing all the steps in the synthesis, therefore applicant's argument is null.

With regards to 3), 4), 6) and 7), Examiner notes that it has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR:

> When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).
>
> The "problem" facing those in the art was the solid phase synthesis of peptides using microwave technologies, and there were a limited number of methodologies available to do so. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In the instant case, the use of different types of resins (which are *functional* solid phase resin *analogs*) and of synthetic steps within the peptide synthesis (which are *complementary synthetic steps*) and one skill in the art would know that the solid phase resins could be substituted for each other and that the steps were complementary towards the goal of a peptide synthesis, in light of the disclosures of Martin and Cargill that teach solid-phase synthesis of peptides in microwave transparent vessels using microwave to accelerate the overall process and in light of the microwave-accelerated individual steps of deprotection, activation and coupling as set forth above for Yu, Williams, Stadler and Santagada. Thus, a process for the solid phase synthesis of peptides which encompasses the use of a microwave transparent vessel and the known solid peptide synthesis steps of deprotection, activation and coupling is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.
>
> In addition, KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness.

See the recent Board decision Ex parte Smith, --USPQ2d--, slip op. at 20, (Bd. Patt. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2s at 1396) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

With regards to 5) please note that Martin's vessel is made of glass, which transmits microwaves. Also, as mentioned above, the term "microwave transparent

vessel" does not exclude other elements from the vessel, therefore the "sandwich dielectric chip" still reads upon a "microwave transparent vessel".

With regards to 8) and 9), please note that the "sandwich dielectric chip" reads upon vessel and the "cellulosic SPOTS membrane" reads upon the solid phase resin.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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